Paper No. 26

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ANDREW D. SUTTON and
RICHARD A. JOHNSON

Appeal No. 1999-2230
Application 08/465,236

HEARD: August 9, 2001

Before WINTERS, MILLS, and GRIMES, Administrative Patent Judges.

WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This appeal was taken from the examiner's decision rejecting claims 22 through 60, which are all of the claims remaining in the application.

Representative Claims

Claims 22, 23, 24, and 28, which are illustrative of the subject matter on appeal, read as follows:

22. Microcapsules, suitable for intra-arterial administration, being hollow and enclosing a gas- or vapor-filled space essentially without solid material therein and being capable of being dried to form a powder of such microcapsules, in which more than 30% of the microcapsules have a diameter within a 2 ：m range and at least 90% have a diameter within the ranges 12.0-25.0 ：m. [Emphasis added.]

23. Microcapsules, suitable for intra-arterial administration, being hollow and enclosing a gas- or vapor-filled space essentially without solid material therein and being capable of being dried to form a powder of such mircocapsules, in which the interquartile range of diameters is 2 ：m or less and the median diameter is between 12.0 ：m and 25.0 ：m inclusive. [Emphasis added.]

24. A pharmaceutical composition suitable for intra-arterial administration, comprising hollow microcapsules of which at least 90% have a diameter of 12.0-25.0 ：m, and at least 30% have a diameter within a 2 ：m range essentially without solid material therein and being capable of being dried to form a powder of such microcapsules. [Emphasis added.]

28. A process comprising the step of atomizing a solution or dispersion of a wall-forming material in a liquid carrier into a gas in order to obtain hollow microcapsules by evaporation of the liquid carrier, wherein said microcapsules are suitable for intra-arterial administration, at least 90% of the microcapsules are 12.0-25.0 ：m in diameter, and at least 30% have a diameter within a 2 ：m range. [Emphasis added.]

The References

In rejecting the appealed claims on prior art grounds, the examiner relies on the following references:

Sands	4,420,442	Dec. 13, 1983
Erbel et al. (Erbel)	5,137,928	Aug. 11, 1992
Mathiowitz et al. (Mathiowitz)	5,271,961	Dec. 21, 1993

The Issue

The issue presented for review is whether the examiner erred in rejecting claims 22 through 60 under 35 U.S.C. § 103 as unpatentable over the combined disclosures of Sands, Erbel, and Mathiowitz.

Deliberations

Our deliberations in this matter have included evaluation and review of the following materials:

(1) the instant specification, including Figures 1 through 5, and all of the claims on appeal;

(2) applicants' Appeal Brief (Paper No. 20) and Reply Brief (Paper No. 22);

(3) the Examiner's Answer (Paper No. 21);

(4) the above-cited prior art references; and

(5) the Osborne Declaration, filed under the provisions of 37 CFR § 1.132, executed June 4, 1998.

On consideration of the record, including the above-listed materials, we reverse the examiner's rejection under 35 U.S.C. § 103.

Discussion

The present invention relates to the preparation of ultrasound contrast agents comprising hollow microcapsules, used to enhance ultrasound imaging techniques. More specifically, the invention relates to hollow microcapsules enclosing a gas- or vapor-filled space essentially without solid material therein, where more than 30% of the microcapsules have a diameter within a 2 ：m range and at least 90% have a diameter within the range 12.0-25.0 ：m. The microcapsules are suitable for intra-arterial administration, and are capable of being dried to form a powder of such microcapsules. The present invention further relates to a process for preparing such microcapsules, and to pharmaceutical compositions comprising the microcapsules.

Prior art echocontrast agents suffer from several drawbacks making them unsuitable for perfusion mapping of the myocardium or similar capillary beds, including poorly controlled size distribution, low pressure resistance, and weak echogencity. In contrast, the microcapsules of the present invention possess unique properties which make them particularly advantageous for use as a deposit echocontrast agent to delineate under-perfused areas of microcirculation. The novel microcapsules are produced by a spray-drying process wherein the median size and size distribution of the microcapsules are tightly controlled. Applicants have discovered that by manipulating the parameters of

the spray-drying process, they are able to produce microcapsules having a unique combination of size, pressure resistance, and size distribution. This unique combination of characteristics results in mircocapsules said to be outstanding deposit echocontrast agents.

As can be seen from a review of representative claims 22, 23, 24, and 28, the claims before us recite microcapsules where "at least 30%" or "more than 30%" of the microcapsules have a diameter within a 2 ：m range, and at least 90% have a diameter of 12.0-25.0 ：m; or "the interquartile range of diameters is 2 ：m or less and the median diameter is between 12.0 ：m and 25.0 ：m inclusive." Having carefully reviewed the content of Sands, Erbel, and Mathiowitz, we find that the combined disclosures of cited references are insufficient to support a conclusion of obviousness of claims containing those numerical limitations.

Sands discloses hollow microspheres, prepared by spray-drying, having a particle size of about 1 to 500 microns (column 2, lines 27 through 30; column 3, lines 51 through 53). The Sands process is said to produce microspheres having particle diameters in the range of "about 1 to 500 microns," suggesting that size distribution of this product is poorly controlled (Osborne Declaration, page 2, paragraph 5). In contrast, the numerical limitations in the claims before us reflect that applicants' hollow microcapsules have a tightly controlled size distribution.

Erbel discloses ultrasonic contrast agents composed of microparticles which contain a gas and polyamino-dicarboxylic acid-co-imide derivatives; processes for their preparation; and their use as diagnostic and therapeutic agents. Based on our review of this reference, we find that Erbel's microparticles have significantly smaller particle sizes compared with the microcapsules recited in the appealed claims. See particularly, Erbel, column 7, lines 15 through 30; and column 10, Table 1. Neither Erbel nor Sands discloses or suggests the numerical limitations on size and size distribution recited in the appealed claims.

In the Answer, paragraph bridging pages 4 and 5, the examiner considerably overstates the significance of teachings found in Mathiowitz. The examiner's position to the contrary, notwithstanding, Mathiowitz does not disclose the preparation of protein microspheres by spray-drying. Mathiowitz does not disclose a method "which is basically the same as the instant method" (Examiner's Answer, page 5, line 12), but rather discloses the preparation of protein microspheres by a phase separation, solvent removal process. Nor does Mathiowitz disclose or suggest the numerical limitations on size and size distribution recited in the claims before us. Viewing the situation in this light, we find that

(1) Mathiowitz does not disclose a product which reasonably appears to be identical with or only slightly different than applicants' claimed microcapsules; and

(2) the examiner has not established an adequate evidentiary basis on this record to shift the burden of proof to applicants under principles of law set forth in In re Fitzgerald, 619

F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980); and In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977). See the Examiner's Answer, page 5, lines 14-18.

In view of the numerical limiations on size and size distribution recited in all of the appealed claims, we disagree that the combined disclosures of Sands, Erbel, and Mathiowitz would have led a person having ordinary skill in the art to the claimed invention. The examiner's decision, rejecting claims 22 through 60 under 35 U.S.C. § 103, is reversed.

REVERSED

Sherman D. Winters Administrative Patent Judge	)
Demetra J. Mills Administrative Patent Judge	) BOARD OF PATENT)) APPEALS AND)) INTERFERENCES
Eric Grimes Administrative Patent Judge	)

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